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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,614	02/06/2006	Stefan Golz	Le A 36 493	6701
35969	7590	10/03/2007	EXAMINER	
JEFFREY M. GREENMAN			LONG, SCOTT	
BAYER PHARMACEUTICALS CORPORATION			ART UNIT	PAPER NUMBER
400 MORGAN LANE			1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/537,614	GOLZ ET AL.
	Examiner Scott D. Long	Art Unit 1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 31 July 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-12 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-4, 6 and 8-12 is/are rejected.
- 7) Claim(s) 1 and 7 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The examiner acknowledges the claim amendments and applicant's remarks, filed 31 July 2007.

Claim Status

Claims 1-12 are pending. Claim 5 is cancelled. Claims 1-4 and 6-10 are amended. Claims 11-12 are newly submitted. Claims 1-12 are under current examination.

Priority

This application claims benefit as a 371 of PCT/EP03/13281 (filed 11/26/2003). The application also claims benefit from the foreign (German) patent application 10257354.9 (filed 12/9/2002). The instant application has been granted the benefit date, 9 December 2002, from the German application 10257354.9.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – 35 USC 112, second paragraph

Applicant's arguments (Remarks, filed 7/31/2007, page 4) and Claim amendments, filed 31 July 2007, with respect to claims 1-3, 7 and 10 have been fully considered and are persuasive. The rejections of Claims 1-3, 7 and 10 under 35 USC 112, second paragraph, have been made moot by the claim amendments submitted on 31 July 2007 and are hereby withdrawn.

Response to Arguments – 35 USC 112, first paragraph (written description)

Applicant's arguments (Remarks, pages 4-6) and claim amendments filed 31 July 2007 regarding rejection of claims 1-3 and 6-9 have been fully considered but they are only partially persuasive.

The applicant correctly construed the examiner's meaning that claim 1(a) and 1(b) were not subject to rejection under 35 USC 112, 1st paragraph (written description) in the previous action. The cancellation of two portions of claim 1 (previously identified as 1(d) and 1(f)) has made moot the written description rejection of these portions of claim 1.

The applicant makes three different arguments: (1) rejection of pending claim 1(d) does not conform to Written Description Guidelines, particularly example 14; (2) Example 9 of the Written Description Guidelines supports the applicant's assertion of possession of the claimed genus encompassed by pending claim 1(c); and (3) the amendments to claims 6-9 overcome the rejection by further limiting the scope of the claimed genus.

Regarding argument 1, the examiner notes that the fact pattern of the instant application does not match that of example 14 of the Written Description Guidelines (WDG). In example 14, the "specification exemplifies a protein isolated...that catalyzes the reaction of A → B" (WDG, Example 14: Product by Function). Additionally, example 14 of the WDG provides a sample claim, "a protein having SEQ ID NO:3 and

variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B.” In the case of pending claim 1(d), the language is similar, “a nucleic acid molecule comprising a sequence which is a least 95% homologous to SEQ ID NO:1 and which encodes a fluorescent protein.” The difference between the fact patterns of Example 14 and the instant claim 1(d) is that the enzymatic activity of the instantly claimed protein is not adequately described in the pending claims 1(d).

Figures 4-5, indicate the Excitation and Emission profiles of the fluorescent protein SEQ ID NO:2. Conceivably, this could be used in an “assay for detecting the catalytic activity of the protein,” as required by Example 14. The Excitation/Emission profiles of SEQ ID NO:2 are very unique and specific and would not be identical to the profiles of other fluorescent proteins. For this reason, the examiner believes that the applicant is not in possession of mutants/variants which have the same expression profile as SEQ ID NO:2 and share at least 95% homology. The applicant has not provided a single example of such a variant. Since it is known in the art that even relatively minor amino acid substitutions can change a green fluorescent protein to a red fluorescent protein (which would have a different catalytic activity), the examiner believes the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention commensurate to the scope of the genus of claim 1(d) encompassing nucleic acids having 95% homology to SEQ IDNO:1 and encoding any type of fluorescent protein at the time the application was filed. The examiner believes that he has described the essential difference that sets the Example 14 and the instant claim apart. Because of this difference, the examiner asserts the instant

application fail to satisfy the guidelines. Therefore, the examiner maintains the rejection of claim 1(d) under 35 USC 112, 1st paragraph (written description) for the reasons of record and the discussion above.

Regarding argument 2, the examiner notes that the fact pattern of the instant application does not match that of example 9 of the Written Description Guidelines (WDG). The essential difference between the facts of Example 9 and those of the instant application is that in the case of Example 9 of WDG, the nucleic acids isolated through highly stringent hybridization methods were subsequently "shown to encode proteins...[that display] activity [identical to that encoded by the example's SEQ ID NO:1]." In addition, the Example notes that "these sequences may or may not be the same as SEQ ID NO:1." Since not all of the isolated nucleic acids of Example 9 have the necessary activity, the adequately described claims were written to reflect that particular sequences had been isolated, though not sequenced, and which also had been shown to encode the necessary activity. In the case of the instant application, the claimed genus of sequences have neither been explicitly disclosed (except SEQ ID NO:1), nor shown to encode the particular excitation/emission activity of SEQ ID NO:2. The examiner feels that this is the essential difference that sets the two apart and therefore causes the instant applicant fail to satisfy the guidelines. Therefore, the examiner maintains the rejection of pending claim 1(c) under 35 USC 112, 1st paragraph (written description) for the reasons of record and the discussion above.

Regarding argument 3, the examiner disagrees with the applicant. The applicant argues that amended claims 6-8 "meet all the written description requirement for the

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reason discussed above" (Remarks, page 6). Claim 6 is directed to an isolated protein encoded by the nucleic acid of claim 1. Claim 1 encompasses a large number of polynucleotides which can encode a large number of polypeptides; as described in the discussions of arguments 1 and 2, the examiner has maintained the rejection of claim 1 under written description. Therefore, the breadth of the genus of polypeptides encompassed by claim 6 and produced by methods of claims 7-8 is not supported by the instant specification. Therefore, the examiner maintains the rejection of pending claims 6-8 under 35 USC 112, 1st paragraph (written description) for the reasons of record and the discussion above.

The applicant has amended claim 9 to change the nature of the claimed product from peptides to antibodies. Therefore, the scope of the written description rejection is moot. Therefore, the examiner hereby withdraws the rejection of claim 9 under 35 USC 112, 1st paragraph (written description).

Considering the potentially large numbers of polynucleotides encompassed by these claims, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed.

Therefore, the examiner maintains the rejection of pending claims 1-3 and 6-8 under 35 USC 112, 1st paragraph (written description) for the reasons of record and the discussion above.

Response to Arguments - Claim Rejections 35 USC § 101

Applicant's arguments (Remarks, filed 7/31/2007, page 6-7) and Claim amendments, filed 31 July 2007, with respect to claims 1-6 and 7-10 have been fully considered and are persuasive. The rejections of Claims 1-6 and 7-10 under 35 USC 101, have been made moot by the claim amendments submitted on 31 July 2007 and are hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 102

Applicant's arguments (Remarks, pages 7-8) and claim amendments filed 31 July 2007 have been fully considered and they are partially persuasive.

The rejection of Claim 5 under 35 USC 102(b) as anticipated by Michaels (US-6,096,865, issued 1 August 2000), has been made moot by the claim amendments submitted on 31 July 2007 and is hereby withdrawn.

The applicant traverses the rejection of claim 6-9 under 35 U.S.C. 102(b) as being anticipated by Levine et al (Compar. Biochem. Physiol. B, 1982. 72;1:77-86) by arguing that "the instantly claimed protein is not the same protein as phialidin" (Remarks, page 8). After re-reading the prior Action (filed 3/6/2007), it appears that the examiner had confused some aspects of the teachings of Levine et al. Levine et al. isolated two distinct proteins, a calcium-activated photoprotein, "phialidin" and a protein described as Phialidium GFP (P-GFP). In the prior action, the examiner wrote, "Levine et al. teach a green fluorescent protein (phialidin, also known as clytin) isolated from

Phialidium gregarium. This is the same protein taught by the instant specification as coming from the same organism with the alternate name, *Clytia gregaria.*" (Action, filed 3/6/2007, page 10). According to Levine et al., the green fluorescent protein and phialidin are not the same protein. Despite the ambiguity of the examiner's previous written statements, the examiner continues to believe that the green fluorescent protein isolated by Levine et al. is the same as SEQ ID NO:2 of the instant application. To support this conclusion, the examiner points out the similarity of Excitation and Emission spectra for the instantly claimed protein having a sequence of SEQ ID NO:2 and that of the isolated P-GFP of Levine et al. Figures 4-5 of the instant specification show the Excitation and Emission profiles for SEQ ID NO:2. In these diagrams, the peak of excitation seems to be slightly greater than 475nm and the peak of emission seems to be slightly greater than 493nm. Levine et al. teach, "The corrected fluorescence excitation spectrum for P-GFP shows a maximum at 487nm and a shoulder near 470nm....The emission spectrum...has a maximum at 497nm and a broad shoulder in the 530-540nm range. With the exception of two unpublished accounts, this represents the first case of a coelenterate green-fluorescent protein having an emission peak at any wavelength other than the characteristic 508-509 nm region." (page 79, col.2). Essentially, both the green fluorescent protein isolated by Levine and SEQ ID NO:2 have the same fluorescence characteristics and are isolated from the same organism. The examiner, therefore, concludes that these are the same protein.

The applicant has amended claims 7-8 so as to clearly claim a method of producing recombinant proteins produced from the nucleic acids of claim 1. Levine et

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al. do not teach recombinant biotechnological methods. Therefore, the rejection of claims 7-8 under 35 U.S.C. 102(b) as being anticipated by Levine et al (Compar. Biochem. Physiol. B, 1982. 72;1:77-86) is hereby withdrawn.

In conclusion, the examiner hereby maintains rejection of claim 6 under 35 U.S.C. 102(b) as being anticipated by Levine et al (Compar. Biochem. Physiol. B, 1982. 72;1:77-86) by

NEW GROUNDS OF REJECTION AND OBJECTION

Claim Objections

Claim 1(d) is objected to because of the following informalities: As a result of amendment, it appears that there is a duplication of the sub-claim designator, "d)". Appropriate correction is required.

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 recites the limitation "vector of claim 11" in part (i) of claim 7. Claim 11 does not precede claim 7. The examiner suggests canceling claim 7 and resubmitting it as claim 13; so doing would solve this dependency problem.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 USC § 112, p 1 "Written Description" Requirement*; (Federal Register/Vol 66.

No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claim 9 is broadly drawn, such that it applies to any a genus of antibodies which specifically bind to the fluorescent protein encoded by isolated nucleic acids encoding

SEQ ID NO:2, encoding proteins that are 95% identical to SEQ ID NO:1, or a variety of fluorescent proteins encoded by nucleic acids which hybridize with SEQ ID NO:1.

The specification does not have a single example of an antibody which specifically binds to SEQ ID NO:2 and certainly does not support possession of a genus of antibodies which specifically bind to the large genus of fluorescent proteins encompassed by claim 6.

Considering the potentially large numbers of antibodies encompassed by these claims, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Claim 10 is directed to a method of determining whether a gene of interest, or fragment thereof, has been expressed comprising monitoring the fluorescence of a polypeptide encoded by a fusion gene and comparing it to the fluorescence when the gene or fragment is not expressed, wherein said fusion gene comprises the nucleic acid of claim 1 operably linked to said gene of interest, or fragment thereof.

The instant specification does not disclose a method as claimed in claim 10.

Therefore, it is new matter.

Claims 4 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 USC § 112, p 1 "Written Description" Requirement; (Federal Register/Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.).*)

Claim 4 is broadly drawn such that it applies to a genus of host cells comprising a expression vectors comprising nucleic acid molecules encoding fluorescent molecules having 95% (1-d) homology with SEQ ID NO:1. Likewise, claim 4 is also drawn to a

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genus of host cells comprising expression vectors comprising nucleic acid molecules which hybridize with SEQ ID NO:1 or differ from SEQ ID NO:1 because of degeneracy of the genetic code. Since there are no examples of sequences that meet the criteria of claim 1c-d provided in the instant application, there can be no host cells comprising expression vectors which satisfy claim 4.

Claims 10-12 are broadly drawn, such that they apply to a genus expression vectors comprising nucleic acid molecules encoding fluorescent molecules having 95% (1-d) homology with SEQ ID NO:1. Likewise, claims 11-12 are also drawn to a genus expression vectors comprising nucleic acid molecules which hybridize with SEQ ID NO:1 or differ from SEQ ID NO:1 because of degeneracy of the genetic code. Since there are no examples of sequences that meet the criteria of claim 1c-d provided in the instant application, there can be no expression vectors which satisfy claims 10-11.

Further discussion of claims 1(c) and 1(d) can be found above in the maintained written description.

The Revised Interim Guideline for Examination of Patent Applications under 35 USC § 112, p1 "Written Description" Requirement (Federal Register/ Vol 66. No 4, Friday January 5, 2001) states "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH

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EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (column 2, page 71436, emphasis added).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION OF THE INVENTION. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, WHATEVER IS NOW CLAIMED." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize the [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Considering the potentially large numbers of host cells and expression vectors comprising polynucleotides encompassed by these claims, the disclosure is not sufficient to show that a skilled artisan would recognize that the applicant was in possession of the claimed invention (genus) commensurate to its scope at the time the application was filed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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